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Mapping and Prediction of Coal Workers' Pneumoconiosis with Bioavailable Iron Content in the Bituminous Coals

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Abbreviations: BAI: Bioavailable iron; COPD: Chronic obstructive pulmonary disease; CWP: Coal workers' pneumoconiosis; USGS: US Geological Survey; NSCWP: National Study of Coal Workers' Pneumoconiosis.

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Abstract:

Based on the first National Study of Coal Workers' Pneumoconiosis (CWP) and the US Geological Survey database of coal quality, we show that the prevalence of CWP in seven coalmine regions correlates with levels of bioavailable iron (BAI) in the coals from that particular region [correlation coefficient $r=0.94$, $p<0.0015$]. CWP prevalence is also correlated with contents of pyritic sulfur ($r=0.91$, $p<0.0048$) or total iron ($r=0.85$, $p<0.016$), but not with coal rank ($r=0.59$, $p<0.16$) or silica ($r=0.28$, $p<0.54$). BAI was calculated using our model taking into account chemical interactions of pyrite, sulfuric acid, calcite, and total iron. That is, iron present in coals can become bioavailable by pyrite oxidation, which produces ferrous sulfate and sulfuric acid. Calcite is the major component in coals that neutralizes the available acid and inhibits iron's bioavailability. Therefore, levels of BAI in the coals are determined by the available amounts of acid after neutralization of calcite and the amount of total iron in the coals. Using the linear fit of CWP prevalence and the calculated BAI in the seven coalmine regions, we have derived and mapped seven thousand coal samples' pneumoconiotic potencies. Our studies indicate that levels of BAI in the coals may be used for the prediction of coal's toxicity, even before large-scale mining.

Introduction:

Coal remains a major energy resource worldwide. In the US, more than 50% of electricity is generated in coal-fired power plants. Recent debate in the US has focused on increasing coal use. In fact, energy costs from a new coal power plant are low, between 3.5 and 4 cents per kilowatt-hour (Jacobson and Masters 2001). However, coal mining causes environmental problems, such as acid mine drainage, while the inhaled coal particles at the work place may lead to the development of coal workers' pneumoconiosis (CWP) (Castranova and Vallyathan 2000; Demchak et al. 2004). According to the newly released Work-related Lung Disease Surveillance Report, CWP deaths accounted for half of the pneumoconiosis deaths during the 10-year period from 1990 to 1999 (NIOSH 2003). Coal mining can also increase the risk of developing asthma and chronic obstructive pulmonary disease (COPD), such as emphysema and chronic bronchitis (Ruckley et al. 1984; Attfield and Kuempel 2003; Soutar et al. 2004). Among the occupations listed by the Census Industry Code, coal mining is the highest risk job associated with asthma and COPD death with a proportionate mortality ratio of 1.98 (95% confidence interval 1.84-2.12, adjusted for age, sex and race), as compared to the second highest risk job of trucking service of 1.29 (95% CI 1.22-1.37) (NIOSH 2003). Federal "Black Lung" Program payments totaled more than $1.5 billion for nearly 190,000 beneficiaries in 1999. Health and environmental costs, such as occupational lung disease compensation, can bring the total cost from 3.5-4 to as high as 5.5-8.3 cents per kilowatt-hour. If we can predict coal's toxicity before mining, we may be able to develop screening and prevention programs that carefully monitor early adverse effects and, thus, reduce healthcare costs related to the coal use.

Coal is an aggregate of heterogeneous substances composed of organic and inorganic materials. The four major coal types ranked in order of increasing heat value are lignite, sub-bituminous, bituminous, and anthracite. The inorganic portion of coal can range from a few percent to more than 50% (by weight) and is composed of phyllosilicates (kaolinite, illite, etc.),

quartz, carbonates, sulfides, sulfates, and other minerals (Meyers 1982). In general, Al and Fe are the main metals in the coals. As, Ni, Zn, Cd, Co, Cu are trace metals that represent only a very small fraction of the mineral matter (Finkelman 1995).

Iron is the best-known transition metal capable of producing oxidants through Fenton, Haber-Weiss, or autoxidation reactions (Huang 2003). However, not all iron compounds in the coals are bioavailable for oxidant formation and subsequent adverse health effects. We have previously defined bioavailable iron (BAI) as the iron released in 10 mM phosphate solution, pH 4.5, which mimics the phagolysosomes of cells (Huang et al. 1998). Based on thirty coal samples from three coalmine regions, we have shown that levels of BAI in the coals correlated with the prevalence of CWP, and it was the BAI in the coals that transactivated the two important transcription factors of activator protein-1 and nuclear factor of activated T cells (Huang et al. 2002; Zhang et al. 2002; Zhang and Huang 2002).

The purpose of this study has been to validate our hypothesis on BAI using a model based on various chemical interactions in the mixed coal dusts. Since it is impossible to obtain and measure BAI in all coal samples from the period when epidemiological studies were performed during 1969 and 1971, the US Geological Survey (USGS) database of coal quality were used for calculating BAI in each coalmine region. USGS database is the largest publicly available database containing information on the chemistry and properties of US coals (Bragg et al. 1998). For each individual coal, molar amounts of pyritic sulfur per gram of dry coal, as well as sulfate, calcium oxide, and total iron were taken into account for the calculation of BAI. Besides BAI, other factors that were previously thought to contribute to CWP were also incorporated, such as coal rank or quartz, for correlation with CWP prevalence. It was shown that CWP prevalence in seven coalmine regions significantly correlated with the levels of BAI from the same region. Using the model that we have developed, seven thousands coal samples' pneumoconiotic potencies were derived and mapped in the present study.

Materials and Methods:

No chemical reagents were used in the present study.

Our hypothesis has been that BAI is the active component in the coals that induces CWP. If that proves to be the case, then the differences in the levels of BAI in the coals may be responsible for the observed regional differences in the prevalence of CWP. To test our hypothesis, CWP prevalence data from the first National Study of CWP (NSCWP) as well as physico-chemical data from USGS coal quality database were used. In 1969, the first round of the NSCWP selected thirty-one coalmines, of which twenty-nine were bituminous, while two were anthracite mines (Morgan et al. 1973). Eight mines were located in Pennsylvania (two anthracite, six bituminous), nine in West Virginia, three in Kentucky, two each in Virginia, Alabama, Illinois, and Utah, and one each in Ohio, Indiana, and Colorado. Participation in the first round was 90.5%. A total of 9,076 miners were fully examined, of which 8,553 were bituminous and 523 were anthracite workers. Because the properties of anthracite are different from bituminous coals and the number of anthracite miners was small, the two anthracite mines in the PA coalmine region was excluded from the present study. Only bituminous coals, including the six in the PA, were used for BAI calculation and its correlation with CWP prevalence.

Based on the names of the coalmines, counties, and states, we have searched the USGS coal quality database and have been able to match ninety-four coal samples from twenty-four coalmines within seven states. These are bituminous coals obtained from mines within the same state, county, and coal seam as those samples used in the first NSCWP. Most of the samples in the USGS database were collected in the period of 1975-1985. The principles of BAI calculation are as follows:

BAI mainly consists of water-soluble iron, such as ferrous and ferric sulfate, which can be originally present in the coals or can be obtained by the oxidation of pyrite (FeS_2). Another possible source of BAI is acid solubilization of siderite ($FeCO_3$) or ferrous silicate ($FeSiO_3$). Using

the USGS coal database, we have calculated levels of BAI in each coal. Considering that the majority of BAI originates from pyrite oxidation (Huggins et al. 1983), we have used the following formula for the calculations:

$$2FeS_2 + 7O_2 + 2H_2O \rightarrow 2FeSO_4 + 2H_2SO_4 \qquad (1)$$

It can be seen that one molar of pyrite will produce one mole of BAI as ferrous sulfate and one mole of sulfuric acid. However, levels of pyrite in the USGS coal database were not measured directly. Since only pyritic sulfur content is available in the database, reaction (1) shows that one mole of pyritic sulfur will produce half a mole of BAI and half a mole of sulfuric acid.

Previous studies have shown that BAI is stable only in an acidic environment (Huang et al. 1994). If there is calcite in the coal, calcite will consume the acid and neutralize the pH as follows:

$$CaCO_3 + H_2SO_4 \rightarrow CaSO_4 + H_2O + CO_2 \qquad (2)$$

Increasing the pH would facilitate ferrous and ferric ion oxidation to goethite (FeOOH), which is water-insoluble and, thus, not bioavailable for redox reactions (Singer and Stumm 1969; Lowson 1982). Therefore, no BAI will accumulate when calcite is present. If calcite is absent in the coals, sulfuric acid produced from reaction (1) would solubilize other iron compounds (*e.g.,* $FeCO_3$) and release more BAI as follows:

$$FeCO_3 + H_2SO_4 \rightarrow FeSO_4 + H_2O + CO_2 \qquad (3)$$

Based on the above chemical reactions, we concluded that the total available molar amounts of sulfuric acid in a given amount of coal would be [H_2SO_4] = [½ pyritic sulfur (S_{py})+ sulfate – calcite]. If [H_2SO_4] $\leq$ 0, this indicates that acid is completely consumed by calcite and, concomitantly, iron will be oxidized. Therefore, there will be no BAI in that coal. If [H_2SO_4] > 0, the excess acid would stabilize BAI and, possibly, also leach out other iron compounds, such as siderite, thus releasing additional BAI.

Based on the USGS coal database, pyritic sulfur and sulfates as percents of coal are available for calculations. Calcite and siderite in the coals were not measured. However, levels of calcium oxide (CaO) and the total amount of iron (shown as Fe_2O_3) were measured in high temperature ashes of the coals and the ash yield in the coal is also available from the USGS database. We assumed that the calcium oxide was all derived from calcite and the iron was derived from pyrite, two of the most common minerals in coal, thus maximizing the calcite and pyrite estimates. Since one mole of CaO is formed by the decomposition of one mole of calcite at high temperature, this allowed us to use the same molar amounts of CaO as measures of calcite. We have then calculated the millimolar amounts of pyritic sulfur and sulfates per 100 g dry coal in each individual coal. The millimolar amounts of CaO and total iron (Fe_2O_3) per 100 g dry coal were also calculated after taking into consideration the ash yield in each individual coal.

Results:

Table 1 shows that marked regional differences in the prevalence of CWP existed with the disease being most common in bituminous miners of Pennsylvania (cumulated prevalence of 45.4%, including diseases of categories 1, 2, 3, and progressive massive fibrosis) and least common in miners of Colorado (4.6%), after adjusting age and years spent underground (Morgan et al. 1973). The follow-up studies at the same mines (in 1972-1975, 1977-1981, 1985-1988 and 1996-2002) have shown that the overall prevalence of CWP decreased in the US due to the lowered dust levels, but the regional difference persisted with a greater risk in Eastern coal miners (PA and WV) than in western coal miners (UT and Colorado) (Attfield and Morring 1992a; Attfield and Seixas 1995; Goodwin and Attfield 1998; Anonymous 2003). After taking into consideration the slight differences present in exposure concentration or mining techniques, as well as the X-ray reader variation or changes in X-ray standard, these epidemiological results indicate that physico-chemical characteristics of the coals responsible for toxicity are different in the Eastern and Western States (Attfield and Morring 1992a). Table 1 also summarizes the

molar ratio of C/H as one of the indicators of coal rank, pyritic sulfur, sulfate, silicon dioxide content, calcium oxide, iron oxide, arsenic, and nickel (millimoles per 100 gram dry coal) from the USGS coal quality database. The sample sizes varied from one State to another because of the availability of coal samples in the USGS database. There were also wide variations on physico-chemical characteristics, as reflected by large standard deviations, which were probably due to the heterogeneity of coal samples. It can be seen that levels of coal rank and silica content, two parameters that were previously thought important in contributing to CWP development, do not vary as much as CWP prevalence does from the East to the West (Table 1). Calcium oxide (CaO), a product from the decomposition of calcite ($CaCO_3$) in the high temperature ashes of the coals, does not differ much from one State to another. In general, levels of pyritic sulfur, total iron, As, and Ni are higher in the Eastern coalmine regions (PA, OH, KT, WV) than in Western coalmine regions (UT and CO).

The average levels of total sulfuric acid (1/2 S_{py} + sulfate), amount of acid available for solubilization of other iron compounds (1/2 S_{py} + sulfate – calcium oxide), total iron, and BAI in each coalmine region are summarized in Table 2. To calculate BAI, we have discovered that the amount of BAI in the coal should be equal to the lesser value between the amount of available acid (1/2 S_{py} + SO_4^{2-} - CaO) and Fe_2O_3, because: 1) if the coal has an excessive amount of acid and a limited amount of iron, BAI will be limited by the amount of iron present; 2) if the coal has less acid but more iron present, BAI will then be limited by the amount of acid since excess iron cannot be solubilized and, therefore, cannot become bioavailable. Table 2 shows the average levels of BAI (millimoles/100 g dry coal) from 7 states with corresponding CWP prevalence reported in the first NSCWP.

Table 3 shows a very good correlation between CWP prevalence and BAI (correlation coefficient r=0.94, 95% CI 0.66-0.999, p<0.0015), as well as with pyritic sulfur (r=0.91, 95% CI 0.35-0.99, p<0.0048), and total iron (r=0.85, 95% CI 0.20-0.97, p<0.016), but not significantly

with coal rank (r=0.59, 95% CI -0.26-0.91, p<0.16) or silica (r=0.28, 95% CI -0.55-0.82, p<0.54). No association of CWP with CaO itself was observed (r= -0.18, 95% CI -0.78-0.60, p<0.69).

The relationship between CWP and BAI is well described by a linear model. Figure 1 displays the fitted line and a scatterplot of the data tagged by the coalmine region of its origin. Based on the levels of BAI in each coal that we calculated with the method mentioned above, we have derived each coal's pneumoconiotic potency in seven thousand coal samples collected by the USGS. Figure 2 shows that there is a geographic distribution of coals with different levels of BAI and, therefore, possibly different pneumoconiotic potencies. For example, in the Western States, most coals do not have BAI, which may pose less risk to coalminers, as shown in green color. In the Eastern States, there is a trend for possibly high risk coals (black and gray color), ranging from PA to OH to WV and KY. There is also an apparent trend of low risk coal (blue and green color) from WV to TN to AL. Since CWP prevalence was much higher at the first round of the NSCWP than the current epidemiological data, the prevalence of CWP in the map is probably overestimated, in part due to reduced dust exposure. However, the indication of the relative risk of CWP in coal mining in various coalmine regions may still be valid and useful for CWP prediction. For example, today most of US coals come from Wyoming, a state that was not studied in the first round of NSCWP, but a low CWP prevalence is predicted in Figure 2.

Discussion:

CWP is one of the occupational diseases that has been most studied by epidemiologists. It has been shown in the USA, Great Britain, France, and Germany that the prevalence and severity of CWP differed markedly among different coalmines despite comparable exposures to respirable dust. In the US, there has been a decline in the prevalence from East to West, the disease being most common in PA coalminers and least common in coalminers from UT. In France, coal miners of Provence never had reported CWP (0%) and the prevalence of CWP in coal miners of Nord Pas de Calais was 24% (Amoudru 1987). In Great Britain, the proportional

mortality ratios for CWP varied from 135 in Leicestershire county to 3825 in South Glamorgan county (Coggon et al. 1995). These epidemiological results indicate that physico-chemical characteristics of the coals responsible for toxicity may be different from one coalmine region to another. This fact allowed us to correlate certain physico-chemical characteristics of coals with the epidemiological results.

Our present study showed a significant correlation between CWP prevalence and levels of BAI in the coals. Pyrite, a typical contaminant in the coals, readily undergoes oxidation and forms BAI and acid. It is well known that the formed acid in the coalmines causes acid mine drainage in the environment and calcite is used for its treatment (Cravotta 2003; Aziz et al. 2004; Demchak et al. 2004). Burning of pyritic sulfur-containing coal produces sulfuric dioxide (SO_2), a major component of acid rain (Srivastava and Jozewicz 2001; Carmichael et al. 2002). BAI, a fraction of total iron, can catalyze oxidant formation and lead to oxidative lung damage. Calcite, a mineral existing only in certain coals, such as those in the Western coalmines, can oxidize BAI and make iron less bioavailable for adverse health effects (Huang et al. 1998; Huang et al. 2002; Zhang et al. 2002; Zhang and Huang 2002). Therefore, our results indicate that certain minerals in the coals can interact and, thus, contribute to different levels of BAI. This might provide an explanation for the observed regional differences in the prevalence of CWP and the associated COPD. Increasing evidence demonstrates that iron present in the coal fly ash, asbestos, or urban particles can lead to increased oxidant, ferritin, and cytokine formation (Chao et al. 1994; Fang and Aust 1997; Smith and Aust 1997; Smith et al. 2000). These studies support our hypothesis that BAI may be responsible for coal dust-induced lung injury.

It is interesting to note that pyritic sulfur and total iron also significantly correlate with CWP prevalence in the present study (Table 3), suggesting that pyritic sulfur and total iron levels, which are available in the USGS coal database, may be used as simple indexes for predicting coal's toxicity. However, we have previously noticed that samples from the coalmines of

Provence, France, had high levels of pyrite (Huang et al. 1994), but coal workers in the Provence coalmine region do not have reported CWP (Amoudru 1987). It is this observation that leads us to search for other factor(s), which may contribute or inhibit CWP development. In fact, the coals of Provence contain large amounts of calcite ($\geq$10% w/w). By suspending these coals in acid (100 mM H_2SO_4), no BAI was released. Therefore, it may not be coincidental that the coals having no BAI did not report CWP in miners working in the coalmine regions. Similarly, coals from UT did not release iron at pH 4.5 mimicking phagalososomes but released iron in 50 mM HCl. These results suggest that not all iron compounds are bioavailable. In fact, the presence of calcite in certain coals is the factor that makes iron less bioavailable. Our results indicate that oxidation of pyrite and subsequent neutralization of acid by calcite is most likely determinants of the levels of BAI in the coal dusts. This is further supported by the improved correlation between CWP prevalence and BAI over the correlation with available acid (1/2 S_{py} + SO_4^{2-} - CaO) or total iron. From a chemical point of view, calcite is more basic than siderite ($FeCO_3$) consuming acid first before siderite. Therefore, calcite limits iron's bioavailability. This should not be surprising since in nutrition, it has long been known that calcium carbonate supplements depress iron's bioavailability (Cook et al. 1991; Prather and Miller 1992; Wienk et al. 1996).

CWP, which was originally thought to be a variant of silicosis, results from the inhalation of coalmine dust that usually contains relatively small amounts of free crystalline silica (quartz) (Castranova and Vallyathan 2000; Borm and Tran 2002). Coal rank was found to play a role, since CWP risk increases with coal rank (Maclaren et al. 1989; Attfield and Morring 1992b). Laboratory coal breakage studies have shown a positive correlation with the amount of respirable-size particles found in the product increasing with coal rank (Moore and Bise 1984). It has been suggested that higher rank coals with a higher electrostatic charge on breakage may contribute to the increased incidence of CWP in the high rank coal regions (Page and Organiscak 2000). However, a correlation between coal rank and cell cytotoxicity has not yet

been established in biological studies (Christian and Nelson 1978; Christian et al. 1979). In the present study, No significant correlation between CWP prevalence and coal rank or silica was observed ($r=0.59$, $p<0.16$ for coal rank and $r=0.28$, $p<0.54$ for silica).

Based on the present study using the calculated model of BAI, we believe that it may be possible to predict which coal is likely to be toxic, even before large-scale mining. However, this study is far from concluding the cause-and-effect of BAI in CWP and the associated COPD development. Further studies on the role of BAI in cell and lung injury as well as the protective role of calcite in inhibiting BAI and the associated injuries are still needed. Other limits of the present study are: 1) non-inclusion of anthracite coals for the correlation study but only bituminous coals, which restricts the usefulness of comparing BAI with coal rank or extrapolation to anthracite coals; 2) incomplete coal samples from all states as in the first NSCWP and no recognition of many coal mines in the Western States (*e.g.,* Wyoming and Texas) being surface mines where CWP may be less likely to occur than in underground coalmines; 3) and lack of consideration of coal particle sizes, effects of other transition metals which may become bioavailable, and the effects of phagolysosomes of cells in contributing to acid solubilization of iron in the coals.

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Figure Legends:

Figure 1. Correlation between prevalence of CWP and BAI in seven US States coalmine regions. The numbers of coal samples per state for which analytical data were available are shown in parentheses.

Figure 2. Mapping and prediction of coal's pneumoconiotic potency by the level of BAI in the coal (Top left: Alaska coalmine region).

Table 1. Information on CWP prevalence, selection of coalmines, average levels of physico-chemical characteristics of coal samples from each coalmine region[a]

State	# of mines	# of samples	CWP (%)	MR (C/H)	SiO_2	CaO	Pyritic Sulfur	SO_4	Fe_2O_3	As	Ni
PA	3	9	45.35	1.28 ± 0.12	71.05 ± 46.22	3.97 ± 2.13	34.76 ± 21.88	1.23 ± 1.06	12.48 ± 7.4	0.33 ± 0.4	0.26 ± 0.17
OH	1	6	31.80	1.09 ± 0.07	84.66 ± 26.96	5.23 ± 7.17	37.08 ± 20.03	1.37 ± 1.20	12.86 ± 8.8	0.17 ± 0.13	0.14 ± 0.19
KY	4	13	29.00	1.20 ± 0.07	69.82 ± 24.06	5.69 ± 9.70	25.48 ± 30.53	0.43 ± 0.6	9.78 ± 9.11	0.15 ± 0.22	0.22 ± 0.11
WV	4	8	28.25	1.32 ± 0.13	49.53 ± 24.00	4.58 ± 3.17	17.89 ± 29.57	0.21 ± 0.21	7.27 ± 8.22	0.22 ± 0.25	0.13 ± 0.05
AL	1	13	16.70	1.26 ± 0.07	71.84 ± 49.59	2.88 ± 2.96	17.07 ± 19.74	0.11 ± 0.99	8.85 ± 5.86	0.40 ± 0.29	0.17 ± 0.13
UT	2	4	13.10	1.08 ± 0.07	40.82 ± 8.51	7.33 ± 5.27	7.97 ± 4.35	0.16 ± 0.06	2.69 ± 2.61	0.01 ± 0.00	0.03 ± 0.00
CO	9	41	4.60	1.04 ± 0.06	117.3 ± 82.53	4.61 ± 2.3	3.43 ± 3.08	0.21 ± 0.14	3.68 ± 1.86	0.03 ± 0.05	0.07 ± 0.06

a. Units are millimolar amount per 100 g dry coal. MR: Molar ratio.

Table 2. Average levels of total sulfuric acid (1/2 S_{py} + SO_4), available amount of acid (1/2 S_{py} + SO_4 - CaO), total iron, and predicted BAI[a]

STATE	# of Mines	CWP (%)	$S_{py}/2 + SO_4$	$S_{py}/2 + SO_4 - CaO$[b,c]	Fe_2O_3	BAI[d]
PA	9	45.35	18.61	14.63	12.48	11.82
OH	6	31.80	19.91	14.69	12.86	9.07
KY	13	29.00	13.17	7.49	9.78	6.25
WV	8	28.25	9.15	4.57	7.27	4.77
AL	13	16.70	9.65	6.77	8.85	5.29
UT	4	13.10	4.14	-3.19	2.69	1.09
CO	41	4.60	1.92	-2.69	3.68	0.15

a. Units for the chemicals are millimoles per 100 gram dry coal. Levels of pyrytic sulfur, sulfate, CaO, and Fe_2O_3 were obtained from the USGS database for each coalmine.

b. CaO was presented as % of high temperature ashes in the USGS database and was converted to % of dry coal before based on the ash yield. Since one mole of calcite ($CaCO_3$) produces one mole of CaO in the ashes, the molar amount of CaO per 100 g coal was used as a measure of $CaCO_3$ levels in the coals.

c. Values in the individual coal samples were calculated first and then averaged for the coalmine region for each of physico-chemical parameters listed in the Table.

d. BAI was calculated as follows: if the difference in [1/2 S_{py} + SO_4 – CaO] is $\leq$ 0 for the individual coalmine, a zero was entered for BAI. If the difference in [1/2 S_{py} + SO_4 – CaO] is > 0, a lesser value between [1/2 S_{py} + SO_4 – CaO] or total iron (Fe_2O_3) is chosen for BAI (see reasons in the text).

Table 3. Correlation among average levels of various parameters with CWP prevalence

	C/H	SiO_2	CaO	Pyritic Sulfur	SO_4^{2-}	$S_{py}/2 + SO_4^{2-}$	$S_{py}/2 + SO_4^{2-}$ - CaO	Fe_2O_3	BAI
R-Value	0.59	0.28	-0.18	0.91	0.58	0.90	0.87	0.85	0.94
Lower 95% CI	-0.26	-0.55	-0.78	+0.35	-0.26	0.40	0.25	0.20	0.66
Upper 95% CI	+0.91	+0.82	+0.60	+0.99	+0.90	0.99	0.98	0.97	0.999
P-Value	0.16	0.54	0.69	0.0048	0.17	0.006	0.01	0.016	0.0015

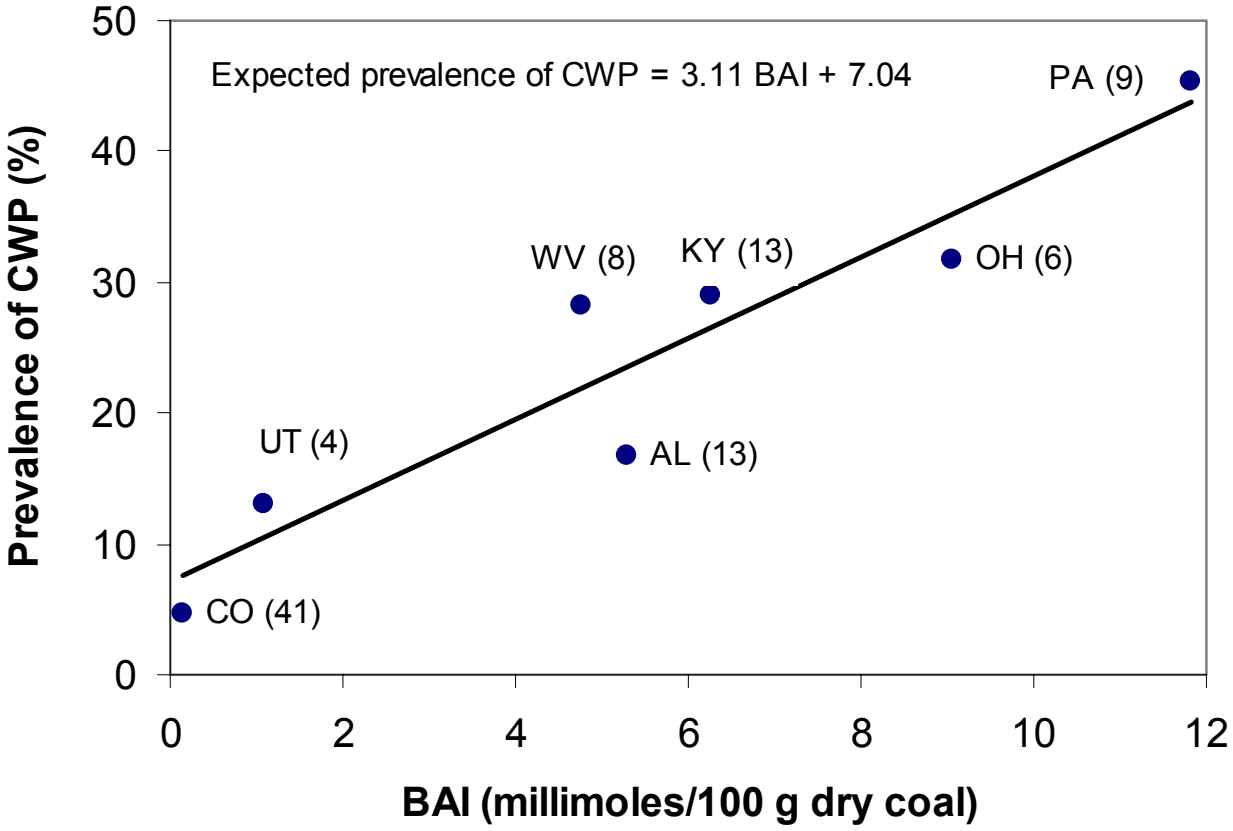

Figure 1. Huang et al.

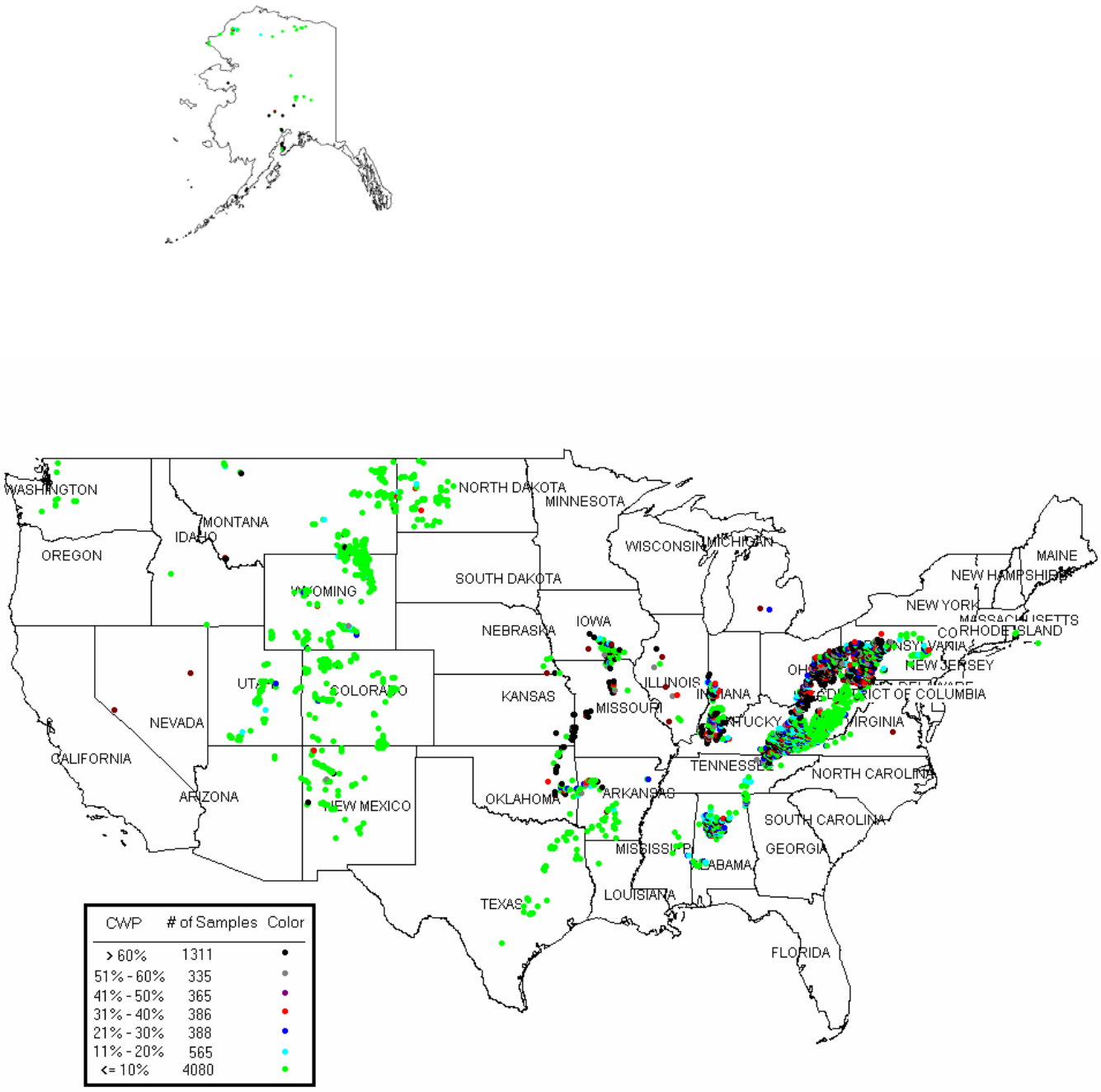

Figure 2. Huang et al.